Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION

Device Generic Name:	A solid-phase chemiluminescent enzyme immunoassay for the qualitative detection of IgM antibody to Hepatitis B core antigen
Device Trade Name:	IMMULITE® Anti-HBc IgM IMMULITE® 2000 Anti-HBc IgM
Applicant's Name and Address:	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, California 90045-5597

Premarket Approval Application (PMA) Number: P010053

Date of Panel Recommendation: None

Date of Notice of Approval to the Applicant: July 26, 2002

II. INDICATIONS FOR USE

IMMULITE Anti-HBc IgM

IMMULITE Anti-HBc IgM is a solid-phase chemiluminescent enzyme immunoassay designed for use on the IMMULITE automated immunoassay analyzer for the qualitative measurement of IgM antibody to hepatitis B core antigen (anti-HBc IgM) in human serum or plasma (EDTA, heparinized, citrate). It is intended for in vitro diagnostic use for the laboratory diagnosis of acute or recent (usually within six months) hepatitis B viral infection.

IMMULITE 2000 Anti-HBc IgM

IMMULITE 2000 Anti-HBc IgM is a solid-phase chemiluminescent enzyme immunoassay designed for use on the IMMULITE 2000 automated immunoassay analyzer for the qualitative measurement of IgM antibody to hepatitis B core antigen (anti-HBc IgM) in human serum or plasma (EDTA, heparinized, citrate). It is intended for in vitro diagnostic use for the laboratory diagnosis of acute or recent (usually within six months) hepatitis B viral infection.

III. DEVICE DESCRIPTION

The IMMULITE and IMMULITE 2000 Anti-Hepatitis B Core IgM Antigen kits are the subject of this PMA. The data and information are presented separately for each assay in this document.

The IMMULITE and IMMULITE 2000 Anti-Hepatitis B Core IgM Antigen kits are solid phase, two step chemiluminescent enzyme immunoassays designed for use on the automated IMMULITE and IMMULITE 2000 analyzers, for the qualitative measurement of IgM antibodies against hepatitis B core antigen in human serum or plasma. The kits are intended for *in vitro* diagnostic use as an aid in the laboratory diagnosis of acute or recent hepatitis B viral infection.

The kits' solid phase is a polystyrene bead coated with a monoclonal murine anti-IgM antibody. The patient sample and a protein-based buffer are simultaneously introduced into the Test Unit or reaction tube and incubated for approximately 30 minutes at 37ºC with intermittent agitation. During this time, HBc IgM in the patient sample binds to the monoclonal, anti-IgM antibody coated bead. Unbound serum is then removed by a centrifugal wash. An alkaline phosphatase-labeled recombinant HBc antigen is introduced, and the reaction tube is incubated with agitation for another 30 minute cycle, during which time the HBc antigen binds to the patient's anti-HBc antibody which is bound to the anti-IgM antibody coated bead. The unbound enzyme conjugate is removed by a centrifugal wash. After the wash, a chemiluminescent substrate is added, and the reaction tube is incubated with agitation for a further 5 – 10 minutes.

The chemiluminescent substrate is a phosphate ester of adamantyl dioxetane which undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous productions of these intermediates results in the sustained emission of light. The bound complex and the resulting photon output, measured as cps by the photomultiplier tube, are related to the presence of HBc IgM antibodies in the sample. A qualitative result is then obtained by comparing the patient results to a stored curve.

IV. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

There are no known contraindications for the IMMULITE Anti-HBc IgM and the IMMULITE 2000 Anti-HBc IgM assay.

Warning and precautions for users of the IMMULITE Anti-HBc IgM and IMMULITE 2000 Anti-HBc IgM assays are stated in the product labeling.

V. ALTERNATIVE PRACTICES OR PROCEDURES

The early assays of IgM antibodies to hepatitis B core antigen (IgM anti-HBc) were based on the principle of immune adherence hemagglutination. These assays were

largely supplanted by radioimmunoassay (RIA) and enzyme immunoassay (EIA) methodologies, which were considered more sensitive, and reproducible. IgM antibody – specific molecules were originally detected either by immunosubtration of IgG in the sample prior to testing or by using anti-human IgM conjugates.

These procedures have been replaced by the IgM capture immunosorbent assays (RIA and ELISA). In capture assays, anti-human IgM (chain-specific) bound to the solid phase is first used to capture IgM in the sample. Detection of specific IgM is then accomplished by the addition of assay-specific antisera and enzyme-labeled anti-HBc conjugate. Because interference from rheumatoid factor or specific IgG antibodies is minimized, the IgM-capture assays usually have better clinical and analytical sensitivity and specificity. There are currently a variety of commercially available, FDA licensed or approved serological tests. When anti-HBc IgM test results are used in combination with supplemental clinical laboratory serological testing, a laboratory diagnosis of HBV infection with HBV can be established. A clinical diagnosis is based on clinical findings, biochemical testing, and serological findings.

VI. MARKETING HISTORY

IMMULITE Anti-HBc IgM and IMMULITE 2000 Anti-HBc IgM have been marketed internationally as an aid in the determination of acute and chronic hepatitis B virus infection since June 1999. IMMULITE and IMMULITE 2000 Anti-HBc IgM have received European Union CE Mark approval and have been marketed in Europe since June 2001. The devices have not been withdrawn from any country for reasons related to safety and effectiveness.

VII. POTENTIAL ADVERSE EFFECTS OF DEVICE ON HEALTH

Potential adverse effects from this device on health can be caused by inaccurate test results and a misdiagnosis. False Negative results can occur when blood specimens are obtained from a subject infected with hepatitis B prior to the appearance of IgM antibody. This may likely result in the patient misdiagnosed as not being infected. Additionally, specimens obtained after the disappearance of anti-HBc IgM antibodies, in the absence of test results for other hepatitis B markers, may have False Positive results and lead to misdiagnosis of a hepatitis B infected patient.

VIII. SUMMARY OF NON CLINICAL STUDIES

Analytical Specificity

Analytical specificity was evaluated at two clinical sites in the United States and at one European site. In the United States, serum specimens from 17 subgroups of patients with potentially cross-reacting microorganisms or conditions were tested by IMMULITE

Anti-HBc IgM, IMMULITE 2000 Anti-HBc IgM, and a commercially available microparticle enzyme immunoassay for anti-HBc IgM (Kit A). The results are displayed in the package insert.

In the European study, four rubella IgM positive specimens, six antinuclear antibody (ANA) positive specimens, and 26 rheumatoid factor (RF) positive specimens were tested by IMMULITE Anti-HBc IgM. IMMULITE Anti-HBc IgM test results were negative for all specimens. The specimens were also tested by IMMULITE 2000 Anti-HBc IgM. The results are shown in the package insert.

In the European study, four rubella IgM positive specimens, five antinuclear antibody (ANA) positive specimens, and 23 rheumatoid factor (RF) positive specimens were tested by IMMULITE 2000 Anti-HBc IgM. IMMULITE 2000 Anti-HBc IgM test results were negative for all specimens.

Calibration Range

The calibration range for IMMULITE and IMMULITE 2000 Anti-HBc IgM is 2 – 100 U/mL (P.E.I., Paul Ehrlich Institute).

Analytical Sensitivity

The analytical sensitivities were evaluated by testing 20 replicates of each serum and plasma sample. Means and standard deviations were calculated from the counts per second (CPS) for the 20 replicates. The analytical sensitivity, defined as the concentration corresponding to 2 standard deviations above the mean, was established at = 2.0 U/mL (P.E.I., Paul Ehrlich Institute) for IMMULITE and IMMULITE 2000 Anti-HBc IgM.

Effects of Bilirubin, Lipemia and Hemolysis

To simulate moderate and severe icterus, different volumes of each of 6 patient samples ranging from non-detectable to high positive IgM antibodies against hepatitis B core antigen were pipetted into lyophilized unconjugated bilirubin to achieve 2 levels of bilirubin concentrations (10 and 20 mg/dL) for each sample. The spiked and unspiked samples were assayed by the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays. In the IMMULITE Anti-HBc IgM tests, the measurable spiked samples had averages of 96% and 92% recovery for 10 and 20 mg/dL bilirubin concentrations, respectively. In the IMMULITE 2000 Anti-HBc IgM tests, the measurable spiked samples had averages of 99% and 97% recovery for 10 and 20 mg/dL bilirubin concentrations, respectively. This study demonstrated that the measurement of IgM antibodies against hepatitis B core antigen was not affected by the presence of unconjugated bilirubin up to 20 mg/dL.

To simulate mild, moderate and severe hemolysis, the same 6 samples were spiked with hemolysate to achieve final hemoglobin levels of 270, 404 and 540 mg/dL. The samples were assayed, both spiked and unspiked, by the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays. In the IMMULITE Anti-HBc IgM tests, the measurable spiked samples

had averages of 95%, 95% and 97% recovery for 270, 404 and 540 mg/dL hemoglobin concentrations, respectively. In the IMMULITE 2000 Anti-HBc IgM tests, the spiked samples had averages of 102%, 100% and 104% recovery for 270, 404 and 540 mg/dL hemoglobin concentrations, respectively. It was concluded that the measurement of IgM antibodies against hepatitis B core antigen was not affected by the presence of hemoglobin up to 540 mg/dL.

The same 6 samples were each spiked with 4 levels of triglyceride at 500, 1000, 2000 and 3000 mg/dL to evaluate the lipemia effect on the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays. Unspiked and spiked samples were tested by the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays. Since no significant increases of antibody levels were observed in the spiked samples with the increase of triglyceride levels, it was concluded that the measurement of IgM antibodies against hepatitis B core antigen was not affected by the presence of triglycerides.

Hook Effect and Carryover

The hook effect study demonstrated that the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays did not have a hook effect up to at least 175 U/mL. The carryover study demonstrated that the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays did not exhibit a carryover phenomenon when samples were preceded by a sample with a very high titer of IgM antibodies against hepatitis B core antigen

Interfering Substances

A study was conducted to evaluate the effects of interfering substances on IMMULITE and IMMULITE 2000 Anti-HBc IgM assays. Potential interfering substances that included common serum constituents, chemotherapeutic and other drugs were spiked into serum samples with 5 or 6 different levels of anti-HBc IgM. The substances and their test levels (concentration) are listed below.

This study demonstrated that the measurement of IgM antibodies against hepatitis B core antigen by IMMULITE and IMMULITE 2000 Anti-HBc IgM was not affected by the presence of any of the interfering substances listed up to the levels tested.

Interferring Substance	Concentration
HUMAN ALBUMIN	6 g/dL
ASCORBIC ACID	3 mg/dL
ALT	7000 U/L
AST	7000 U/L
ALK PHOSPHATASE	5000 U/L
CORTISONE	400 ug/dL
CYCLOSPORIN A	18.02 ug/dL
GANCICLOVIR	11.8 ug/mL
ETHANOL	350 mg/dL
INTRON A	2730 IU/mL
LAMIVUDINE	20 ug/mL
LDH	6000 U/L
NELFINAVIR	40 ug/mL

Effects of Anticoagulants

The measurement of anti-HBc IgM is not affected by the presence of heparin, sodium citrate, and EDTA anti-coagulants. A study that included 44 specimens collected into plain, heparinized, sodium citrate, and EDTA vacutainer tubes was conducted. The results are shown in the package insert.

Precision

Precision studies for the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays were conducted at three sites. Included in the studies were three controls and seven patient samples covering the entire working range (2 – 100 U/mL) of both assays. All controls and samples were tested in duplicate by three IMMULITE Anti-HBc IgM kit lots and one IMMULITE 2000 Anti-HBc IgM kit lot for a total of 40 runs at each of the three sites.

IMMULITE and IMMULITE 2000 Anti-HBc IgM are qualitative assays with results expressed in U/mL. Statistics including the means, standard deviations, the intraassay and total precision were calculated for samples 2 through 6. Statistics for samples 1 and 7 were not calculated because sample 1 consistently yielded <2 U/mL results and sample 7 consistently yielded results greater than 100 U/mL.

IMMULITE Anti-HBs IgM Intra-assay and Total Precision (U/mL), IMMULITE 2000 Anti-HBs IgM Intra-assay and Total Precision (U/mL), IMMULITE Anti-HBc IgM Lot-to-Lot and Site-to-Site, and IMMULITE 2000 Anti-HBc IgM Site-to-Site Precision data are shown in the package insert.

The IMMULITE 2000 Anti-HBc IgM lot-to-lot precision has not been evaluated. Because lot-to-lot evaluation of the assay had previously been demonstrated, and the Stability studies were done on three lots and the data was acceptable, no additional studies were requested of the sponsor.

EDTA, heparin, and sodium citrate samples were assayed in duplicate in three runs on three days at three U.S. sites for three lots of IMMULITE Anti-HBc IgM and one lot of IMMULITE 2000 Anti-HBc IgM. The median total variance of coefficients (EDTA,

7.7%; heparin, 7.2%; sodium citrate, 8.3%) demonstrated that these alternative sample types do not affect the precision of IMMULITE and IMMULITE 2000 Anti-HBc IgM.

Stability

Stability studies for IMMULITE and IMMULITE 2000 Anti-HBc IgM were conducted by using 3 lots of IMMULITE Anti-HBc IgM, and one lot of IMMULITE 2000 Anti-HBc IgM. The kits and components were subjected to different storage/stress conditions to simulate adverse conditions that might be encountered during shipment and use at clinical laboratories, to establish the long-term (shelf-life) claims, to approximate and support the real time stability and to test the robustness of individual components.

The studies demonstrated that the performance of IMMULITE and IMMULITE 2000 Anti-HBc IgM assays was not affected if properly stored at package insert conditions for at least 720 days.

These studies also demonstrated that the performance of IMMULITE and IMMULITE 2000 Anti-HBc IgM assays was not affected following initial stresses (37°C, or –20°C) for at least 720 days.

IX. SUMMARY OF CLINICAL STUDIES

Expected Values

Individuals acutely infected with the hepatitis B virus develop anti-HBc IgM between two weeks and four months after exposure, usually through the course of clinical illness. IgM antibody levels decline in cases of uncomplicated acute infection, but remain elevated in chronic HBV infection.

Demographics and expected prevalence rates for different categories of subjects (HBV Chronic patients, HBV Acute patients), each of whom provided one specimen, from four clinical studies, one in the northwestern United States (Study 1), two in the southern United States (Study 3, using specimens from China, and Study 4) and one in Europe, are summarized in the package inserts.

Clinical Studies

A total of 815 subjects were tested at four clinical laboratories to assess the performance of the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays when compared to FDA-approved or licensed hepatitis B assays (Reference markers). All specimens in the analyses were initial test results. The specimens were categorized based on the results of testing with the HBV reference serological markers, reactive(+)/ nonreactive(-). No other laboratory or clinical information was used in the disease classification process.

Site 1: Conducted in the northwestern United States, this study included 281 patients, consisting of 138 males and 88 females. Gender for 55 subjects was not reported. These subjects had an average age of 43 years, ranging from 21 to 85 years. Distributions of the ethnicity of the subjects are shown in the following table.

Ethnicity	*N*	%
African American	15	5.3%
Caucasian	169	60.1%
Hispanic	2	0.7%
Asian	32	11.4%
Other	3	1.1%
Unknown	60	21.4%
Total	281	100%

These subjects included acute and chronic hepatitis B patients, vaccinated individuals, pregnant women, and apparently healthy individuals, and patients with potentially crossreactive substances and medical conditions.

A total of 281 specimens were prospectively (n=92) and retrospectively (n=189) collected and tested by FDA-approved or licensed hepatitis B assays for six HBV serological markers (HBsAg, HBeAg, Anti-HBc IgM, Anti-HBc, Anti-HBe, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated 17 unique patterns:

Characterization based on single point specimens	Number of patients	HBV Reference Markers					
		HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	2	+	–	–	–	–	–
Acute	1	+	+	–	–	–	–
Acute	32	+	–	+/-	+	+	–
Acute	34	+	+	+/-	+	–	–
Chronic	2	+	–	–	+	–	–
Chronic	3	+	+/-	–	+	+	+
Chronic	1	+	–	–	+	–	+
Chronic	1	+	+	+/-	+	–	+
Early Recovery	16	–	–	+/-	+	+	+
Early Recovery	4	–	–	–	+	+	–
Early Recovery	19	–	–	–	+	+/-	–
Early Recovery	1	–	–	+	+	+/-	+
HBV vaccine response	27	–	–	–	–	–	+
Not previously infected	120	–	–	–	–	–	–
Recovered	16	–	–	–	+/-	–	+
Recovered	1	–	+/-	–	+	–	+
Uninterpretable	1	–	+	–	–	–	–

Based on the above classifications the IMMULITE Anti-HBc IgM results were compared to Kit A, a reference assay for the determination of anti-HBc IgM.
There were not sufficient patient samples to calculate each Negative and Positive Agreement. However, the Total Positive agreement is 85.7% (6/7) with a 95% CI of 42.1 to 99.6%. The Negative agreement is 97.0% (262/270) with a 95% CI of 94.2 to 98.7%. The Total agreement is 96.8% (268/277) with a 95% CI of 93.9 to 98.5%. This data is in the package insert.

Based on the above classifications the IMMULITE 2000 Anti-HBc IgM results were compared to Kit A, a reference assay for the determination of anti-HBc IgM.
There were not sufficient patient samples to calculate each Negative and Positive Agreement. However, the Total Positive agreement is 85.7% (6/7) with a 95% CI = 42.1 to 99.6%. The Negative agreement is 95.2% (257/270) with a 95% CI of 91.9 to 97.4%. The Total agreement is 94.9% (263/277) with a 95% CI = 91.7 to 97.2%. This data is in the package insert.

Site 2: Conducted in the northeastern United States, this study included 209 patients, consisting of 104 males and 103 females. Gender for two patients was not reported. These patients had an average age of 47 years, ranging from newborn to 93 years. Distributions of the ethnicity of the patients are shown in the following table.

Ethnicity	*N*	%
African American	21	10.0%
Caucasian	101	48.3%
Hispanic	3	1.4%
Asian	6	2.9%
Other	7	3.3%
Unknown	71	34.0%
Total	209	100.0%

Included were patients with potentially crossreactive substances and medical conditions. A total of 209 retrospective specimens were collected and tested by FDA-approved or licensed hepatitis B assays for four HBV serological markers (HBsAg, Anti-HBc IgM, Anti-HBc, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated eight unique patterns:

Characterization based on single point specimens	No. of patients	HBV Reference Markers			
		HBsAg	Anti-HBc IgM	Anti-HBc	Anti-HBs
Acute	8	+	–	–	–
Acute	9	+	+/-	+	–
Chronic	2	+	–	+	+
Early recovery	33	–	+/-	+	+
Early recovery	17	–	–	+	–
HBV vaccine response	32	–	–	–	+
Not previously infected	107	–	–	–	–
Uninterpretable	1	+	–	–	+

Based on the above classifications the IMMULITE Anti-HBc IgM results were compared to Kit A. There were not sufficient patient samples to calculate each Negative and Positive Agreement, or the Total Positive agreement. However, Negative agreement is 99.0% (202/204) with a 95% CI of 96.5 to 99.9%.

Based on the above classifications the IMMULITE Anti-HBc IgM results were compared to Kit A, a reference assay for the determination of anti-HBc IgM. There were not sufficient patient samples to calculate each Negative and Positive Agreement, or the Total Positive agreement. However, the Total Negative agreement is 98.5% (201/204) with a 95% CI of 95.8 to 99.7%. The data is in the package insert.

Site 3: Specimens obtained from China were tested in the southern United States, this study included 79 patients and was comprised of 13 females and 55 males (gender for 11 patients was not reported) with an average age of 36 years, ranging from 18 to 82 years. These were prospectively recruited patients from a clinically well-characterized, homogeneous population: acute hepatitis B patients who presented with symptoms

typical of acute hepatitis B such as jaundice, persistent fatigue, loss of appetite, pale stools and liver enlargement. Their ALT and AST results were significantly elevated at the time of diagnosis.

A total of 79 specimens were prospectively collected and tested by FDA-approved or licensed hepatitis B assays for six HBV serological markers (HBsAg, HBeAg, Anti-HBc IgM, Anti-HBc, Anti-HBeAg, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated 11 unique patterns:

Characterization based on single point specimens	Number of patients	HBV Reference Markers					
		HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc	Anti-HBe	Anti-HBs
Acute	23	+	–	+/-	+	+	–
Acute	8	+	+/-	+	+	+	–
Acute	1	+	–	+	+/-	–	–
Acute	35	+	+	+/-	+	–	–
Acute	4	+	+	+	+	–	+/-
Chronic	1	+	–	–	+	–	–
Chronic	3	+	+/-	–	+	+	–
Chronic	1	+	+	+/-	+	–	+
Chronic	1	+	+	+	+	+	+
Recovered	1	–	–	–	+/-	–	+
Uninterpretable	1	+	–	+	+	+	+

Based on the above classifications the IMMULITE Anti-HBc IgM results were compared to Kit B, a reference assay for the determination of anti-HBc IgM. There were insufficient data to calculate each Negative and Positive Agreement. However the Total Positive agreement is 88.6% (31/35) with a 95% CI of 73.3 to 96.8%. The Negative Agreement is 65.9% (27/41) with a 95% CI of 49.4 to 79.9%. The Total agreement is 76.3% (58/76) with a 95% CI = 65.2 to 85.3%. The data is shown in the package insert.

Based on the above classifications the IMMULITE 2000 Anti-HBc IgM results were compared to Kit B, a reference assay for the determination of anti-HBc IgM. There were not sufficient patient samples to calculate each Negative and Positive Agreement. However, the Total Positive agreement is 91.4% (32/35) with a 95% CI of 76.9 to 98.2% The Negative agreement is 61.0% (25/41) with a 95% CI of 44.5 to 75.8%. The Total agreement is 75.0% (57/76) with a 95% CI of 63.7 to 84.2%. The data is presented in the package insert.

Site 4: Conducted in the southern United States, this study included retrospectively collected specimens from 200 pregnant subjects. These subjects had an average age of 28 years, ranging from 17 to 41 years.

A total of 200 specimens were tested by FDA-approved or licensed hepatitis B assays for four HBV serological markers (HBsAg, Anti-HBc IgM, Anti-HBc, and Anti-HBs). Characterization based on single point specimens by the reference serological markers demonstrated three unique patterns:

Characterization based on single point specimens	Number of subjects	HBV Reference Markers			
		HBsAg	Anti-HBc IgM	Anti-HBc	Anti-HBs
Early recovery	4	–	+/-	+	+
Early recovery	2	–	–	+	–
HBV vaccine response	42*	–	–	–	+
Not previously infected	152*	–	–	–	–

Based on the above classifications the IMMULITE and IMMULITE 2000 Anti-HBc IgM results were compared to Kit B. Note: Five specimens were not tested for IMMULITE Anti-HBc IgM. There were no data points to calculate the Total Positive agreement. The Total Negative agreement is 99.5% (194/195) with a 95% CI of 97.2 to 100.0%. For the IMMULITE 2000 the Total Negative agreement is 99.5% (199/200) with a 95% CI of 97.2 to 100.0%. The data is presented in the package insert.

Site 5: In an additional study conducted in-house at DPC, IMMULITE Anti-HBc IgM was compared to DPC's IMMULITE 2000 Anti-HBc IgM on 46 samples. (Concentration range: approximately 2 to 95 U/mL). By linear regression:

$$(\text{IML } 2000) = 0.99\ (\text{IML}) - 0.34 \ \text{U/mL}$$
$$r = 0.981$$

Slope 95% CI: 0.93, 1.05
Intercept 95% CI: -3.22, 2.54

X. CONCLUSIONS DRAWN FROM STUDIES

The data from both the non-clinical and clinical studies demonstrate acceptable performance is obtained with the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays for the qualitative measurement of IgM antibodies against hepatitis B core antigens in human serum or plasma.

Safety

As a diagnostic test, the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays involve removal of blood from an individual for testing purposes. The test, therefore, presents no more safety hazard to an individual being tested than other tests where blood

is removed. However, misdiagnosis may result when the patient receives a False Positive or False Negative results.

Benefit/Safety

The submitted clinical studies have shown that the IMMULITE and IMMULITE 2000 Anti-HBc IgM assays, when compared to reference clinical laboratory procedures, has a similar ability to detect the presence of IgM anti-HBc in specimens from individuals infected with HBV. The rate of false positivity and false negativity are within acceptable limits compared to the reference assay. It has been shown that the device has no demonstrable cross-reactivity with other viruses or organisms that may cause clinical hepatitis. Therefore, these devices should benefit the physician in the diagnosis of HBV.

Based on the results of the preclinical and clinical laboratory studies the IMMULITE and IMMULITE 2000 Anti-HBc IgM, when used according to the provided directions and in conjunction with other serological and clinical information, should be safe and effective and pose minimal risk to the patient due to false test results.

XI. PANEL RECOMMENDATION

Pursuant to Section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not the subject of an FDA Microbiology Devices Advisory Panel meeting because the information in the PMA substantially duplicated information previously reviewed by this Panel.

XII. CDRH DECISION

FDA issued an approval order on July 26, 2002.

The applicant's manufacturing facility was found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIII. APPROVAL SPECIFICIATIONS

Directions for Use: See labeling

Hazards to Health from Use of the Device: See Contraindications, Warnings, Precautions and Adverse Events in the labeling**.**

Postapproval Requirements and Restrictions: See approval order.